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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,821	02/27/2004	Revital Lifshitz-Liron	1662/62902	8234

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KENYON & KENYON LLP  
ONE BROADWAY  
NEW YORK, NY 10004

EXAMINER
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DESAI, RITA J

ART UNIT	PAPER NUMBER
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1625

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/09/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/789,821	<b>Applicant(s)</b> LIFSHITZ-LIRON ET AL.	
	<b>Examiner</b> Rita J. Desai	<b>Art Unit</b> 1625	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 16 October 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### DETAILED ACTION

Claims 1-12 are pending.

The rejection of claims 1-12 under 35 U.S.C. 103 over US PreGrant 20040181086 102(e) date Kambiz Javdani et al An expt. with acid mine water John Cattaneo 7/2000., eaves US 4594466 1986 and Water treatment Susan Kegley et al still stands.

unpatentable over Hayes, 6.2.2.1, Selective Precipitation, ILIPAC compenadum o chemical Terminology, (IUPAC), chm.vt.edu (VT), Angel C. de Dios, Le Chatelirrs Principle, Lecture VIII, Chem 056 (de Dios), Complexation and Precipitation Titrations (Complexation), Volumetric (Titrametric) Analysis (Volumetric Analysis), Protein purification Handbook (the Handbook), and Solubility of Ionic Salts in Water: Precipitation Titrations (Ionic Salts) for the reasons set forth on pages 2 and 3 of the Office Action mailed 4/13/2006 still stands.

Applicants arguments that the examiner has not provided any references to show that changing the pH brings about precipitation and then it is dried to form recrystallized Zolendronic acid.

The examiner now is providing references.

One of them is the Separation of impurities from leach Liquors 6.2.2 and selective precipitation

6.2.2.1, 1993. Hayes.

The reference teaches separating impurities from a suspension by selective precipitation by controlling and changing the pH. See the whole document which teaches that changing the pH is a common process for precipitaton and removing impurities.


IUPAC Compendium of Chemical Terminology 1997 also defines the precipitation titrations.

Also see chem..vt .edu definition of titration and the relation ship between the pH and

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neutralization.

Le Chateliers Principle also shows that as the pH changes the reaction proceed in one direction and precipitation would occur. Thus as we increase the H ion concentration (lower the pH) the acid in the solution would proceed to go out of the solution and get precipitated out leaving all the basic impurities in solution. Thus a purer acid would be separated. See the lectures by Angel C.de Dios Chem 056.

Zolendronic acid is an acid of the formula  and in a basic solution it would be in solution. The addition of an acid would move the reaction in the direction to precipitate it out.

Also see the principles for Complexation and precipitation Titrations, Volumetric (Titrimetric) Analysis. These references shed some more light with regards to the precipitation reactions. Also see the protein purification handbook, 1997, which teaches more commercial use of changing the pH to precipitate out substances.

Solubility of Ionic Salts in water: Precipitation titrations. Nov. 1996 James Plambeck. Also teaches how salts precipitate out and the common ion effect.

Thus with the above teaching known to a skill in the art it would have been obvious to precipitate out the Zolendronic acid from its basic solution by the addition of an acid solution, thus reducing the pH to obtain the precipitate.

Response to the arguments:

Applicants argue that the reference does not specifically teach the Zolendronic acid.

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Yes that may be correct , however the teaching for the separation and purifying of any acid is clearly taught. ( If it did the rejection would be a 102 rejection) . Crystallization is a process of separation and purification. The limitation added by the amendment has no patentable weight as the term is relative, and the precipitate in the step would inherently be "more" purified than the original crude acid.

Applicants further argue that Le Chateleirs principle titration etc teach that the pH of a solution changes when an acid or base is added, that the mass balance in an equilibrium can be changed by adding a reactant or a product, and that, during a titration, a product may, but does not necessarily, precipitate. However, none of the cited references disclose or suggest that the disclosed principles can be used to purify any specific acid, and, in particular, do not disclose or suggest that the disclosed principles can necessarily be used to purify zoledronic acid.

This is not convincing as the reference does not have to disclose the specific acid but just the principle and the teaching.

Applicants specification clearly states that as used herein, the term "suspension" means undissolved particles in a liquid. The acid in the prior art is recrystallized from water hence it is clear that the acid is soluble in water . The properties of Zolendronic acid states that it is highly soluble in basic solution and slightly soluble in acidic solution , would motivate any person skilled in the art to crystallize and purify it by changing the pH's . Dissolving in basic solution and then precipitation out by lowering the pH.

The rejection still stands.

***Conclusion***

Claims 1-12 still stand rejected.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rita J. Desai  
Primary Examiner  
Art Unit 1625

*RJ Desai*  
1/4/07

R.D.  
January 4, 2007